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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/643,888	08/20/2003	Don J. Diamond	1954-433	4642

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EXAMINER	
MINNIFIELD, NITA M	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 08/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/643,888	DIAMOND, DON J.	
	Examiner	Art Unit	
	N. M. Minnifield	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-4 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-4 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892) 3sheets

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 2/3/04.

4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .

5) ☐ Notice of Informal Patent Application (PTO-152)

6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-4 are pending in the present application.

2. Applicant should update the continuity data found on page 1 of the specification.

3. The use of trademarks has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

4. Claims 1-4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are vague and indefinite in the recitation of vaccine; the claims do not recite what kind of disease or infection this vaccine is to protect against.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are directed to a vaccine, which comprises a peptide selected from the group consisting of SEQ ID NOs: 38, 52 and 64. The vaccine further comprises an adjuvant, DNA adjuvant or CpG DNA.

The peptides of SEQ ID NO: 38, 52 and 64 are human cytomegalovirus (HCMV) peptide of cytotoxic T lymphocyte epitope analogs and the specification states that they have improved immunogenic potency (p. 6). The specification states that the invention provides vaccines comprising such peptides (i.e. cytotoxic T lymphocyte epitope analogs SEQ ID NOs: 38, 52 and 64) (p. 7).

Example 1 of the specification discloses Peptide Synthesis and Characterization (pp. 21-22). Example 2 of the specification discloses the Preparation of Peptide-Loaded Antigen Presenting Cells and *In Vitro* Stimulation (pp. 22-24). Example 3 discloses Derivation of HCMV-Specific T Cell Clones Using Limiting Dilution from IVS Cultures (p. 24). Example 4 of the specification discloses a Chromium Release Assay (pp. 24-25). Example 5 discloses Analysis of Individual Substitutions in Alanine Substituted peptide Ligands (pp. 25-28). Example 6 discloses the Preparation of Positional Scanning Synthetic Combinatorial Library (pp. 28-29). Example 7 of the specification discloses PS-SCL Screen with T cell clone 3-3F4 (pp. 29-34). Example 8 discloses Cytotoxicity of Nonamer peptides Predicted from PS-SCL Screen (pp. 34-35). Example 9 of the specification discloses T Cell Clone Flow-Cytometric

Measurement of HLA-Ig Dimer Binding to T cell clone Mediated by Antigen Analog and Control Peptides (pp. 35-36). Example 10 discloses Recognition of the $pp65_{495-503}$ CTL Epitope by HLA A*0201 Donors (pp. 36-38). Example 11 discloses Enhanced Immunogenicity Peptide Analogs with Retained Universal Recognition (pp. 38-42). Example 12 of the specification discloses Recognition of Antigen Analogs by Multiple T Cell Clones (pp. 42-43). Example 13 discloses MHC Binding Affinity of Antigen Analogs by T2 Assembly Assay (pp. 43-44).

None of the examples set forth in the specification disclose or teach a vaccine comprising the (HCMV) peptide of cytotoxic T lymphocyte epitope analogs, SEQ ID NO: 38, 52 or 64, that was administered to a subject (animal or human) that provided protection against infection and disease caused by HCMV. The specification only sets forth in vitro experimentation that shows that the epitope analogs provide improved immunogenic potency. However, improved immunogenic potency is not equivalent to vaccine protection. The specification has not set forth guidance to one of skill in the art exactly which of these epitope analogs provides vaccine protection, or if any of them can.

The state of the art is unpredictable in this regard and suggests that this is not possible. Diamond et al teaches that in vivo immunization of HLA A2.1 transgenic mice with the MCE peptide will stimulate an immune response, which recognizes and kills HCMV infected human fibroblast. These studies suggest that the HLA A*0201 restricted peptide is a candidate CTL epitope vaccine to prevent or minimize DCMV infection after BMT (pp.1751-1752; materials and methods; p. 1759). Diamond indicates that these peptides may be candidates for a vaccine, not that vaccine protection has been achieved. The prior art states, that "it remains a challenge to develop an efficacious vaccine without live virus to establish long-

term immunity in seronegative individuals". (p. 1763). Zaia et al also discuss the possible use of MCE as immunogens but to date they have not provided vaccine protection. BenMohamed et al teaches the importance of $CD4^+$ T_H lymphocytes in the optimal in vivo induction of CTLs against a representative viral pathogen, indicating that T_H epitopes have to be included in the design of epitope-based vaccine against CMV or other pathogens (p. 776). The teachings of BenMohamed et al appear to suggest that the epitope analogs alone would not be sufficient to provide vaccine protection. In view of the state of the prior art and the lack of guidance in the specification with regard to how to use the claimed vaccine to protect against HCMV infection, there would be undue experimentation required to practice the claimed invention.

7. No claims are allowed.

8. The pending claims recite the presence of specific sequence, SEQ ID Nos: 38, 52 or 64. These sequences are free of the prior art.

9. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to N. M. Minnifield whose telephone number is 571-272-0860. The examiner can normally be reached on M-F (8:00-5:30) Second Friday Off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette R.F. Smith can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

N. M. Minnifield
Primary Examiner
Art Unit 1645

NMM
August 5, 2004